REMARKS

Claims 2-9 are pending. Claims 2-8 are under examination. Withdrawn claim 9 is being maintained of record.

DOUBLE PATENTING

Claims 2-8 have been provisionally rejected on grounds of obviousness-type double patenting as allegedly being unpatentable over claims 1-44 and 46-66 of copending Application No. 11/535,779 (the '779 application). Claims 15-44 and 46-66 have been canceled from the '779 application. Upon an indication of otherwise allowable subject matter applicants will consider filing a terminal disclaimer over the '779 application.

The attention of the Examiner is directed to U.S. Application No. 11/841,508, filed August 20, 2007, and published as US 2008/0015209 A1, which is a continuation of the '779 application.

INVENTION IS ENABLED

Claims 2-8 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly not being enabled by the specification. This rejection is respectfully traversed.

In the instant case applicant has disclosed certain of compounds, has described how to make such compounds, has stated what diseases they are useful for treating, has taught how to formulate and administer such compounds, as well as their dosages. And yet the Office asserts its "position that one skilled in the art could not practice the invention without undue experimentation." (December 12, 2006 Office Action, page 6). In view of the extensive disclosure in this application, the rejection's assertion of undue experimentation presumably means that the Office does not believe that the compounds

recited in the claims are useful in treating the recited diseases when administered as described in the specification.

The Office bears the burden of establishing that an invention does not satisfy the enablement requirement of 35 U.S.C. §112, first paragraph. As stated by the CCPA in In re Marzocchi:

> "As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support."

(In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, ___) (underlining added). It is not sufficient for the Office to simply assert that it doubts the correctness of the statements in the disclosure. The Office must back up its doubts with evidence or reasoning. Again from In re Marzocchi:

> "In any event, it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement."

(In re Marzocchi, 439 F.2d at 224, 169 USPQ at ___) (internal citations omitted) (underlining added). The only reasoning presented by the rejection is the alleged unpredictability of the pharmaceutical art in general. The rejection stated:

> "It is generally recognized in the art that biological compounds often react unpredictably under different circumstances. The relative skill of the artisan or [sic] the unpredictability of the pharmaceutical art is very high."

(December 12, 2006 Office Action, page 3) (internal citations omitted). But that does not constitute adequate reasoning to support an enablement rejection. If the mere assertion that the pharmaceutical art is unpredictable would be accepted as sufficient reasoning, it would mean that in the case of all biological and pharmaceutical inventions applicants would have the burden of demonstrating enablement rather than the Office having the burden of demonstrating that an invention is not enabled. And that would be contrary to the law as articulated in Marzocchi above.

WO 02/100341 (of record) tested and demonstrated the activity of a representative number of compounds within a genus. The person of ordinary skill in the art would accept that other compounds within the genus would possess activity similar to the compounds tested. The Office considers applicants' argument to be unpersuasive because "the instant specification does not teach how the instant compounds are effective in treating one of the diseases from the list [in claim 2] such as diabetes and its various types." (September 10, 2007 Office Action, page 4) (underlining added). The position of the Office is contrary to the law because, "it is axiomatic that an inventor need not comprehend the scientific principles on which the practical effectiveness of his invention rests, nor is the inventor's theory or belief as to how his invention works a necessary element in the specification to satisfy the enablement requirement of 35 U.S.C. §112." Cross v. Iizuka, 753 F.2d 1040, 1042, 224 USPQ 739, ____ (Fed. Cir. 1985), citing Fromson v. Advance Offset Plate, Inc., 720 F.2d 1565, 1570, 219 USPQ 1137, 1140 (Fed. Cir. 1983).

The September 10, 2007 Office Action singled out gestational diabetes as a disorder whose treatment allegedly is not enabled by the specification. The rejection stated:

> Note the enclosed reference, Health Insite, discloses the three major types of diabetes. The three types are type I, type II and gestational.

(September 10, 2007 Office Action, pp. 4-5). Nothing in the cited Health Insite reference gives any reason to doubt the efficacy of the claimed invention in treating gestational diabetes. To the contrary, the reference supports a connection between Type 2 diabetes

and gestational diabetes. The reference states, "Risk factors for GDM [gestational diabetes mellitus] include a family history of diabetes, . . . obesity and being a member of a community or ethnic group with a high risk of developing type 2 diabetes." www.healthinsite.gov.au/topic/Types_of_Diabetes (downloaded 8/31/07). As seen from the reference, obesity is a risk factor for Type 2 diabetes and for gestational diabetes. Moreover, a family history of diabetes or being a member of an ethnic group with a high risk of developing type 2 diabetes is also a risk factor for developing gestational diabetes. Accordingly, the person of skill in the art would have no reason to doubt that the efficacy of the claimed invention in treating type 2 diabetes would hold true for gestational diabetes as well.

The basis of the rejection with respect to treatment of diabetes appears to be that the specification does not contain undue experimental results demonstrating efficacy against gestational diabetes. The rejection stated:

> Applicants' specification does not contain any undue experimentation using the instant compounds of claim 2 are effective in treating gestational diabetes. Clearly, the instant specification shows results in diabetic mice for type I and type II diabetes only.

(September 10, 2007 Office Action, page 5). Of course, a specification need not contain working examples to satisfy the enablement requirement of Section 112, first paragraph. Thus the examples, which are prophetic and accordingly use the present tense, together with the rest of the specification do provide guidance to the person of skill in the art as to how to practice the claimed invention. And there is certainly no basis for imposing a standard that would require a specification to "contain . . . undue experimentation" in order to satisfy the enablement requirement.

The December 12, 2006 rejection singled out cachexia as a disorder whose treatment allegedly is not enabled by the specification. Compounds of the invention reverse insulin resistance associated with diabetes and metabolic disease. While insulin resistance is often associated with obesity (especially in the setting of concurrent hyperinsulinemia), insulin resistance is also a component of disease states involving weight loss (abstract of

Wedick NM, et al. (2001) Insulin resistance precedes weight loss in adults without diabetes. American Journal of Epidemiology 153:1199-1205; abstract of Rofe et al., (1994) Altered insulin response to glucose in weight-losing cancer patients. Anticancer Research 14:647-650.) (of record).

Cachexia involves muscle wasting associated with disease states including cancer, systemic inflammation, infection and aging. A key element in cachexia is impaired insulin sensitivity, especially in muscle. Cancer patients with weight loss often have impaired glucose tolerance, a sign of insulin resistance (Rofe et al., 1994 (abstract); abstract of Tayek, (1992) A review of cancer cachexia and abnormal glucose metabolism in humans with cancer. Journal of the American College of Nutrition 11:445-456) (of record). Insulin signaling in muscle inhibits proteolysis; either insulin deficiency or insulin resistance disinhibits proteolysis, leading to loss of muscle mass. Combined insulin deficiency and resistance occurs in uncontrolled Type 1 diabetes and in cancer cachexia.

An additional link between insulin and body weight dysregulation in both obesity and cachexia is tumor necrosis factor alpha (TNFα). TNFα was originally known as "cachectin" due to its role in cachexia or muscle wasting and weight loss induced by infection and cancer. However, TNFα expressed in adipose tissue induces insulin resistance and obesity (abstract of Argiles et al., (1997) Journey from cachexia to obesity by TNF. The FASEB Journal 11:743-751) (of record). TNFα is one of the causes of insulin resistance in both diabetes and cachexia (abstract of de Alvaro et al., (2004) Tumor Necrosis Factor α produces insulin resistance in skeletal muscle by activation of Inhibitor κB Kinase in a p38 MAPK-dependent manner (2004) Tumor Necrosis Factor α produces insulin resistance in skeletal muscle by activation of Inhibitor κB Kinase in a p38 MAPK-dependent manner) (of record).

Compounds of the invention reverse insulin resistance associated with diabetes and obesity, and can attenuate weight gain in that situation. However, by addressing insulin

resistance in situations where muscle wasting is occurring, including insulin deficiency states, compounds of the invention attenuate the severity of cachexia, both prophylactically and therapeutically.

The preceding argument concerning cachexia was presented in the May 7, 2007 Amendment. The September 10, 2007 Office Action did not specifically repeat the grounds of rejection relating to cachexia, nor did it point to any defect in or otherwise discuss applicants' argument concerning cachexia.

In view of the foregoing, applicants respectfully submit that the enablement rejection has been overcome.

CONCLUSION

In view of the preceding remarks, applicants respectfully request reconsideration and withdrawal of all objections and rejections.

It is believed that no fee is required in connection with the filing of this Communication. If any fee is required, the Commissioner is hereby authorized to charge the amount of such fee to Deposit Account No. 50-1677.

Respectfully submitted,

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